AD_____

Award Number: W81XWH-08-2-0117

TITLE: The STRONG STAR Multidisciplinary PTSD Research Consortium

PRINCIPAL INVESTIGATOR: John D. Roache, Ph.D.

CONTRACTING ORGANIZATION: University of Texas Health Science Center
San Antonio, TX 78229

REPORT DATE: September 2011

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
01-09-2011	Annual	1 SEP 2010-31 AUG 2011

4. TITLE AND SUBTITLE
The STRONG STAR Multidisciplinary PTSD Research Consortium

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-08-2-0117

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
John D. Roache, Ph.D.

E-Mail: roache@uthscsa.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Texas Health Science Center
San Antonio, TX 78229

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The proposed study seeking to identify predictors of differential response to SSRI's is significant given the widespread use of SSRI's. With CDMRP approval, we have revised the aims of the second study to include only an analysis of STRONG STAR Repository data. We have finally begun to recruit subjects in the first study, though the rate of accrual is still not where it needs to be. Protocols and study SOP's have been developed and regulatory approvals have been achieved. STVHCS staff have been trained, though CTVHCS lost staff and need new hires to replace those losses.

15. SUBJECT TERMS

SSRI Antidepressants, Regulatory Approval Delays, Pending Study Enrollment

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	10	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

Page

Introduction……..……..……..4

Body……..5-6

Key Research Accomplishments…….…….…...6

Reportable Outcomes……...6

Conclusion……...…7

References…….……7

Appendices…….……7

Supporting Data……7

INTRODUCTION:

There are two components to this project. The first is a study of the assessment and treatment of alcohol use disorder comorbidity among separated veterans who have PTSD and were exposed to deployment-related trauma. A particularly important aspect of this study is an evaluation of the hypothesis that there are subgroups of patients who have different phenomenological presentations of alcohol use related comorbidity; and further that these subgroups have fundamental differences in their serotonin biology that cause them to respond differently to medication treatment with selective serotonin reuptake inhibitors (SSRI's). These objectives are being approached in two different ways. First, we are conducting a randomized clinical trial evaluating the efficacy of sertraline (an SSRI) in the treatment of PTSD-Alcohol Use Disorder Dual Diagnosis patients who are previously-deployed veterans seeking treatment in the Texas Veterans Health Care System. This is a two-site trial involving both the South Texas and Central Texas Veterans Health Care Systems and it involves dual diagnosis psychotherapy (using the COPE manual) as well as randomized treatment with sertraline vs. placebo.

The second component of the project, involves extending the generality of observations that SSRI's can differentially alter the outcome of treatment for PTSD in different patient subgroups. The original plan was to perform a cluster analysis of patients in treatment in a separate Fluoxetine treatment trial. However, progress on that trial has not been forthcoming. In consultation with DoD Project Officer, Kim DelCarmen, it was determined to satisfy this objective instead through an analysis of the STRONG STAR data repository. Demographic and psychological disturbance information obtained at baseline will assess the phenomenological characteristics of active-duty military personnel receiving treatment for psychiatric symptoms at Fort Hood. These data will be used to perform a cluster analysis of phenomenological types of patients. Subsequent analyses will determine how SSRI use and assessed drinking behaviors may modulate treatment outcome and whether or not the cluster types predict this outcome.

BODY:

- Preparation and Review of the Research Proposal for Multiple IRB Approvals. See Regulatory Action and Milestone Excel spreadsheet for this project.

PI	Organization	Regulatory Action	Submission Date	Approval Date	Date Approval Received	Comments
Roache	UTHSCSA IRB	New Protocol-Administrative Pre-review	1/25/2009	5/8/2009		
Roache	STVHCS	New Protocol Submission	2/2/2009	4/26/2010		
Roache	UTHSCSA IRB	New Protocol-Full-board Review	2/12/2009	5/8/2009		
Roache	STVHCS	Response to Pre-Review	3/4/2009	4/26/2010		
Roache	STVHCS	Response to Stipulations	4/21/2009	4/26/2010		
Roache	UTHSCSA IRB	New Protocol-Response to Full-board Review	4/30/2009	5/8/2009		
Roache	UTHSCSA IRB	New Protocol-Response to Full-board Review (Additional Stips)	5/11/2009	5/8/2009		
Roache	UTHSCSA IRB	Amendment #1	5/29/2009	6/12/2009		see #1 HSC20090236H Human Amendment Form (Protocol and Consent Changes)
Roache	STVHCS	Response to Stipulations	6/9/2009	4/26/2010		
Roache	HRPO	Second Level Review	8/14/2009	11/3/2010		see entire packet at \\echo\strongstarregulatory\STRONG STAR Protocols\Roache Protocol\HRPO\Second Level Review\HRPO packet, Roache, 08-14-09
Roache	DSMB	DSMB Initial Review	8/20/2009	3/28/2011		Reviewed Version 2 February 12, 2009
Roache	BRU	New Protocol Submission	10/2/2009	N/A		
Roache	STVHCS	Response to Stipulations	1/7/2010	4/26/2010		
Roache	UTHSCSA IRB	Amendment #2	1/7/2010	1/29/2010	2/2/2010	#2 Amendment, removed remove Trisha Benson, Crystal Pearson, Christie Ybarra, and Shawn Jones. Added Mascarenas, Gujardo, Murff, polanco, and Hammack. Updated
Roache	BRU	New Protocol Submission	1/14/2010	N/A		
Roache	UTHSCSA IRB	Progress Report-Continuing Review 2010	1/20/2010	3/12/2010	2/23/2010	
Roache	CTVHCS IRB	Protocol Review-Initial	Feb-10	5/12/2010		
Roache	UTHSCSA IRB	Progress Report-Continuing Review 2010 (response to stips)	3/5/2010	3/12/2010	2/23/2010	
Roache	HRPO	Second Level Review	3/23/2010	11/3/2010		
Roache	HRPO	Second Level Review-Response to Stipulations	3/31/2010	11/3/2010		
Roache	STVHCS	Response to Stipulations	4/6/2010	4/26/2010		
Roache	UTHSCSA IRB	Amendment #3	4/6/2010	4/20/2010	4/21/2010	add Dr. Flynn as VA investigator
Roache	STVHCS	Amendment #1	4/27/2010	4/28/2010		#1 Amendment, added VA audio consent.
Roache	HRPO	Second Level Review-Response to Stipulations	4/28/2010	11/3/2010		
Roache	CTVHCS R&D	Protocol Review-Initial	May-10	5/25/2010		
Roache	UTHSCSA IRB	Amendment #4	5/27/2010	6/10/2010	6/14/2010	Add Kenny and Crystal as IE
Roache	STVHCS	Amendment #2	6/1/2010			#2 Amendment, revised study personnel list. Added Belinfante and Mendoza.
Roache	BRU	New Protocol Submission	6/29/2010	N/A		
Roache	HRPO	Second Level Review-Response to Stipulations	7/16/2010	11/3/2010		
Roache	HRPO	Second Level Review-Response to Stipulations	7/27/2010	11/3/2010		
Roache	HRPO	Second Level Review-Response to Stipulations	8/24/2010	11/3/2010		resent on 8/25/10 to update protocol page numbers
Roache	HRPO	Second Level Review-Response to Stipulations	8/25/2010	11/3/2010		previous copy had tracked changes from our last response to stips-revised to include
Roache	HRPO	Second Level Review-Response to Stipulations	9/1/2010	11/3/2010		
Roache	HRPO	Second Level Review-Response to Stipulations	9/20/2010	11/3/2010		
Roache	STVHCS	Amendment #3	10/4/2010	10/22/2010		#3 Amendment, updated VA personnel list (corrseponds with UTHSCSA amendment
Roache	UTHSCSA IRB	Amendment #5	10/4/2010	10/22/2010	10/26/2010	Response to HRPO stips
Roache	STVHCS	Amendment #4	10/19/2010	pending		#4 Amendment, revised VA audio consent. added Dr. Peterson and Dr. Klocek as
Roache	HRPO	Second Level Review-Response to Stipulations	10/26/2010	11/3/2010		
Roache	CTVHCS IRB	Amendment #1	Nov-10	11/17/2010		
Roache	CTVHCS IRB	Amendment #1, response to stips	Nov-10	11/17/2010		
Roache	BRU	Amendment-UTHSCSA Amendment #5	11/4/2010	N/A		#5 Amendment, Version 4 dated 10-4-10 updated study staff, updated inclusion exclusion criteria. Updated recruitment, recruitment material, screening and consent procedures. Added Relief Drinking
Roache	HRPO	Second Level Review-Response to Stipulations	11/17/2010	11/23/2010		Supporting documents for CTVHCS approval
Roache	HRPO	Second Level Review-Response to Stipulations	11/22/2010	11/23/2010		Supporting documents for CTVHCS approval
Roache	UTHSCSA IRB	Amendment #6	1/7/2011	2/14/2011	2/15/2011	updated recruitment material
Roache	UTHSCSA IRB	Progress Report-Continuing Review 2011	1/12/2011	2/22/2011	2/23/2011	
Roache	STVHCS	Continuing Review 2011	1/19/2011	pending		
Roache	UTHSCSA IRB	Progress Report-Continuing Review 2011, response to stips	1/20/2011	2/22/2011	2/23/2011	
Roache	UTHSCSA IRB	Amendment #6 (response to stips)	2/1/2011	2/14/2011	2/15/2011	The VA had been removed from the ads as a site location, and they asked us to put it
Roache	UTHSCSA IRB	Amendment #7	3/14/2011	4/1/2011	4/6/2011	Clarify stopping medications prior to enrollment, revised inc/exc criteria, and clarified
Roache	DSMB	DSMB Initial Review, Response to Stips	3/24/2011	3/28/2011	4/20/2011	
Roache	HRPO	Continuing Review for UTHSCSA 2011	4/7/2011	7/18/2011	7/18/2011	
Roache	CTVHCS IRB	Continuing Review 2011	4/7/2011	6/8/2011		
Roache	UTHSCSA IRB	Amendment #8	4/26/2011	5/3/2011	5/9/2011	Add Malach and Hernandez
Roache	STVHCS	Amendment #5	4/26/2011	5/2/2011	5/2/2011	Add Ann Marie Hernandez and Steffany Malach as therapists at the VA (UTHSCSA
Roache	UTHSCSA IRB	Amendment #9	5/5/2011	6/20/2011	6/20/2011	TV ads
Roache	CTVHCS IRB	Continuing Review 2011, response to stips	5/18/2011	6/8/2011		
Roache	UTHSCSA IRB	Amendment #9, response to stips	6/1/2011	6/20/2011	6/20/2011	revised TV spot per STVHCS Office of Public Affairs
Roache	HRPO	Continuing Review for CTVHCS 2011	6/16/2011	7/18/2011	7/18/2011	
Roache	UTHSCSA IRB	Amendment #10	8/4/2011			Update Inc/Exc criteria (changed min age from 18 to 21, changed heavy drinking days required to 30%, changed alcohol dependence to alcohol use disorder, changed
Roache	UTHSCSA IRB	Amendment #10 Re-Submitted	8/8/2011			

- Hiring and Training of Research Staff. Dr. Roache has developed the study procedures for the treatment protocol and Dr. Javors has done so for the biological assessments required for the study. Mr. Jonathon Polanco is the Study Coordinator in conjunction with Mr. Bill Murff who is overseeing the two-site coordination. Dr. John Klocek is the site PI at the PTSD Center of Excellence at the CTVHCS and Dr. Jennifer Guajardo is the PI at the STVHCS. Drs. Klocek, Guajardo, and Jeslina Raj, Psy.D., have been trained to provide psychotherapy as have two

STRONG STAR Post-Doctoral Fellows and one fellow at the STVHCS. Dr. Klocek will oversee additional and continued Psychologist training for fidelity to the COPE manual. All STVHCS personnel have been trained and are implementing the protocol. The training study coordinator at CTVHCS has terminated employment which has delayed the start of the study at that site.

- Two Site Coordination. Mr. Murff at UTHSCSA is coordinating the two study sites. Dr. Roache, Mr. Murff, and Mr Polanco have all visited the CTVHCS site in Waco to deliver study materials and identify any site needs. For the multisite coordination, we have:
  - Determined how UTHSCSA accounts could be used to compensate subjects in Waco.
  - Provided CTVHCS with study supplies.
  - Provided blood collection and processing equipment and supplies.
  - Arranged for a contract pharmacy to provide compounded, blinded medication to the CTVHCS.
  - Arranged for a blood collection, processing, and shipment protocol to enable the CTVHCS personnel to send specimen samples to San Antonio.

- Participant Recruitment, Therapy, Participant Evaluation. To date six Veterans have been consented and two have been randomized. Because of the difficulty identifying and recruiting eligible OIF/OEF Veterans into this study, several protocol amendments have been implemented to facilitate recruitments, and Dr. Roache and his study team have been visiting VA clinics and distributing study newsletter information to gain clinical patient referrals. In consultation with Dr. del Carmen and Dr. Murray Raskind of the EAB, approved protocol amendments include: a) dropping the OEF/OIF requirement allowing combat veterans from other deployments; and b) dropping the alcohol dependence requirement, allowing alcohol use disorder; and c) direct recruitment of combat veterans from the community. Dr. Roache and his study team have identified 17 clinics within the STVHCS from which potential patients may be referred. We have presented the study at staff meetings, distributed study brochure information, and sent providers a series of Study Newsletter information about dual diagnosis issues within the VA.

- Database, Data Entry, and Data Analysis. The STRONG STAR Data Core has developed our subject enrollment and randomization database, and provided a draft version of the study database. At the time of this report, the final study database programming is being completed and a sample shipping database is being developed.

- Administrative Tasks. Dr. Roache participated in weekly STRONG STAR teleconferences and in monthly calls with Dr. Kim del Carmen. In response to an EAB request to specify subject recruitment milestones, Dr. Roache identified two recent reports (Kranzler et al. 2011a,b) of a study showing differential efficacy of sertraline in the treatment of primary alcohol dependence. Based upon these data, we were able to conduct a new power analysis which suggested the need for much smaller samples than previously proposed. From these analyses, a sample size of n=34 would be required to satisfy Aim #1, and n=100 would be required to satisfy Aim #2.

Key Research Accomplishments

- We have finally begun recruitment and randomization but there have not been other accomplishments.

Reportable Outcomes

- There were no reportable outcomes in the past year.

Conclusion

- The study is actively recruiting in San Antonio and approved for recruitment in Waco. The Center of Excellence in Waco is working with Dr. Klocek to support the study so that patient recruitment and accrual can begin there soon. With the consultation and agreement of Dr. del Carmen and consultant Dr. Raskind, the protocol has been modified to relax the subject Inclusion/Exclusion criteria. Minimum necessary recruitment goals have been specified based upon a new power analysis suggested much smaller sample sizes are required.

References

Kranzler H, et al. (2011a) Comparison of alcoholism subtypes as moderators of the response to sertraline treatment. *Alc Clin Exp Res, in press (privileged communication).*

Kranzler H, et al. (2011b) Post-Treatment outcomes in a double-blind randomized trial of sertraline for alcohol dependence. *Alc Clin Exp Res, in press (privileged communication).*

Appendices

See Attached Regulatory Action and Milestone Chart

Supporting Data

none

2009

Regulatory Action	Submitted / Approved	Jan-09		Feb-09		Mar-09		April-09		May-09		June-09		July-09		August-09		Sep-09		Oct-09		Nov-09		Dec-09	
		Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App
UTHSCSA IRB	Protocol Approval	25									8														
	Protocol Review-Full Board			12							8														
	Protocol Review-response to stips							30			8														
	Protocol Review-response to stips									11	8														
	Amendment #1									29			12												
BRU	Protocol submission-initial																			10	N/A				
HRPO	Second Level Review															14									
STVHCS	Protocol Review-initial			2																					
	Protocol Review-initial, response to pre-review					4																			
	Protocol Review-initial, response to stips							21																	
	Protocol Review-initial, response to stips											9													
DSMB	Initial Review															20									

2010

Regulatory Action	Submitted / Approved	Jan-10		Feb-10		Mar-10		April-10		May-10		June-10		July-10		Aug-10		Sep-10		Oct-10		Nov-10		Dec-10	
		Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App
UTHSCSA IRB	Amendment #2	7	29																						
	Amendment #3							6	20																
	Amendment #4									27		10													
	Amendment #5																			4	22				
	Continuing Review-2010	20					12																		
	Continuing Review-2010, response to stips					5	12																		
BRU	Protocol submission-initial (additional docs)	14	N/A																						
	Protocol submission-initial (additional docs)											29	N/A									4	N/A		
	Amendment (UTHSCSA Amendment #5)																					4	N/A		
HRPO	Second Level Review																						3		
	Second Level Review, additional documents					23																	3		
	Second Level Review-Response to Stipulations					31																	3		
	Second Level Review-Response to Stipulations							28															3		
	Second Level Review-Response to Stipulations													16									3		
	Second Level Review-Response to Stipulations													27									3		
	Second Level Review-Response to Stipulations															24							3		
	Second Level Review-Response to Stipulations															25							3		
	Second Level Review-Response to Stipulations																	1					3		
	Second Level Review-Response to Stipulations																	20					3		
	Second Level Review-Response to Stipulations																			26			3		
	Second Level Review-Response to Stipulations																					17	23		
	Second Level Review-Response to Stipulations																					22	23		
STVHCS	Protocol Review-initial								26																
	Protocol Review-initial, response to pre-review								26																
	Protocol Review-initial, response to stips								26																
	Protocol Review-initial, response to stips								26																

	Protocol Review-initial, response to stips	7							26																
	Protocol Review-initial, response to stips							6	26																
	Amendment #1							27	28																
	Amendment #2											1													
	Amendment #3																			4	22				
	Amendment #4																			19					
CTVHCS IRB	Protocol Review-Initial			Feb							12														
	Amendment #1																					Nov	17		
	Amendment #1, response to stips																					Nov	17		
CTVHCS R&D	Protocol Review-Initial											May	25												

2011	Months	Jan-11		Feb-11		Mar-11		April-11		May-11		June-11		July-11		Aug-11		Sep-11		Oct-11		Nov-11		Dec-11	
	Submitted / Approved	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App	Sub	App
Regulatory Action																									
UTHSCSA IRB	Amendment #6	7			14																				
	Amendment #6, response to stips			1	14																				
	Continuing Review-2011	12			22																				
	Continuing Review-2011, response to stips	20			22																				
	Amendment #7					14			1																
	Amendment #8							26	3																
	Amendment #9									5			20												
	Amendment #9, response to stips											1	20												
	Amendment #10															4									
	Amendment #10 Re-Submitted															8									
HRPO	Continuing Review for UTHSCSA 2011							7							18										
	Continuing Review for CTVHCS 2011											16			18										
STVHCS	Continuing Review-2011	19																							
	Amendment #5							26			2														
CTVHCS IRB	Continuing Review 2011							7					8												
	Continuing Review 2011, response to stips							7					8												
DSMB	Initial Review						28																		
	DSMB Initial Review, Response to Stips					24	28																		
Monthly Target Recruitment		4		5		5		5		6		6		7		7									
Cumulative Target		6		11		16		21		27		33		40		48									

Participants Contacted		1	3	7	5	0	0	6	20				
Participants Screened		1	2	4	6	0	0	5	14				
Participants Consented		0	0	0	1	1	0	2	2				
Excluded After Consent		0	0	0	0	2	0	1	0				
Participants Withdrawn		0	0	0	0	0	0	0	0				
Dual Enrolled		0	0	0	0	0	0	0	2				
Actual Cumulative Enrolled		0	0	0	1	2	2	4	6				

	Date Submitted: Nov.2, 2011
	Date Approved